Remarks

Applicant appreciates the examination of the present application as evidenced by the non-final Office Action dated February 16, 2010 (hereinafter, the "Office Action"). Applicant is also grateful to Examiner Jacob Cheu for participating in a telephone interview on July 13, 2010 (hereinafter, the "interview") with Applicant's U.S. legal representative Shawna Cannon Lemon, Applicant's European representative Dr. Lisa Brown and Applicant Dr. John Colyer.

As noted in the Interview Summary dated July 14, 2010 provided by the Examiner, the participants discussed the pending application, particularly claims 30 and 57. In view of the helpful and constructive dialog expressed during the interview, Applicant sets forth herein remarks and illustrations that support the novelty and nonobviousness of pending Claims 30-52, 54 and 57.

I. Claim Rejection Under 35 U.S.C. § 102

Claim 57 stands rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Publication No. 2003/0059461 to Backer et al. (hereinafter "Backer") and by Prestigiacomo et al. (1995) Scand. J. Clin. Lab. Invest. 55, 57-59 (hereinafter "Prestigiacomo"). *See* Office Action, pages 2 and 3.

Backer

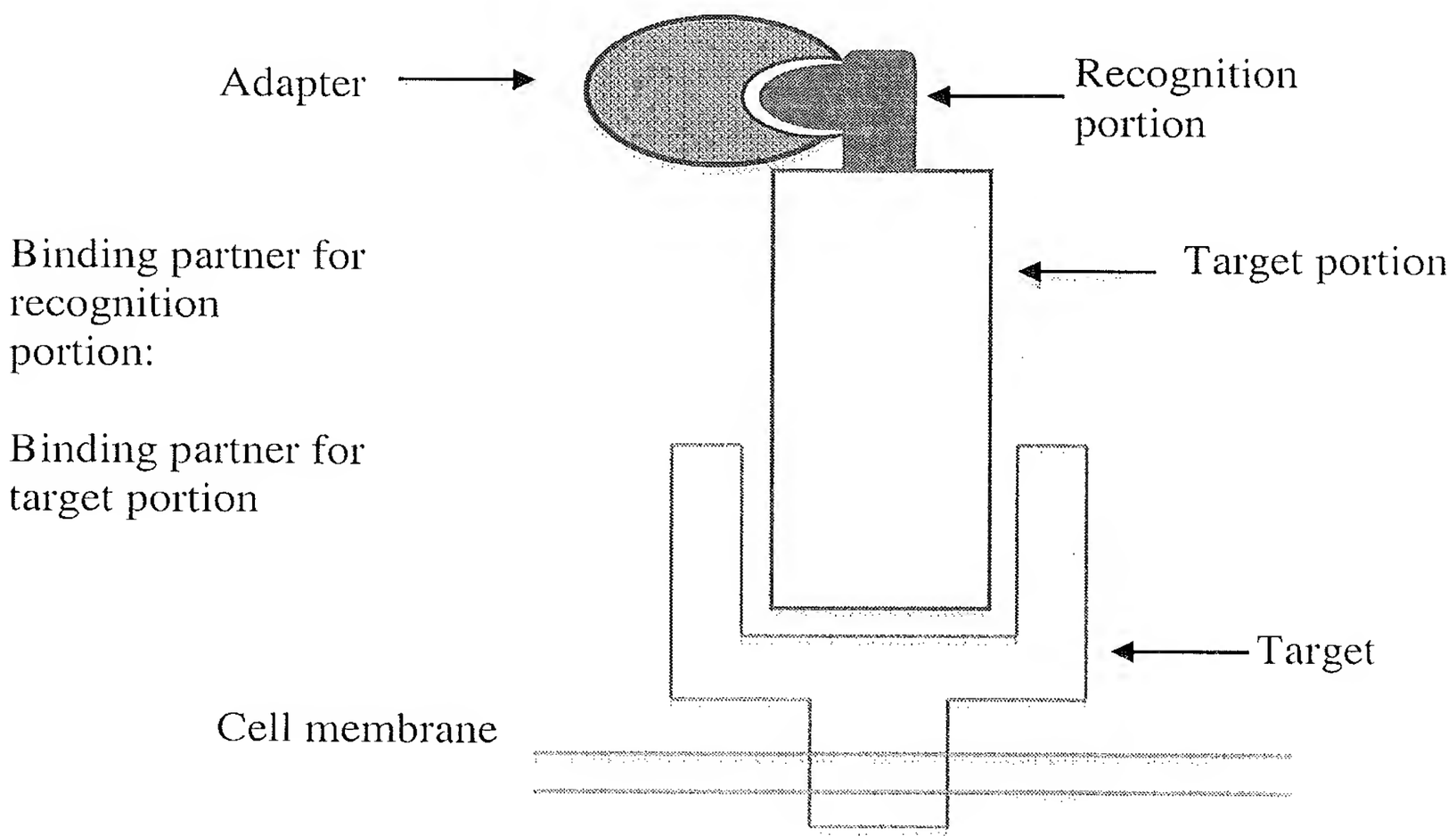
The Office Action states, "Backer et al. teach covalently binding target moiety molecule to S-tag. It is noted that the domain of S-tag containing lysines is for purification purpose and would not interact with the binding partner of target molecule." Office Action, page 3 (citations omitted).

Applicant respectfully submits that Backer describes a presentation system including two parts– a targeting portion and a recognition portion. **Both these parts have binding partners** (the Target and Adapter molecule, respectively, *see* FIG. 1A and illustration below) and binding of each binding partner to the respective part of the presentation system is **essential for the performance of the technology described in Backer** (*see*, for example, Backer, claim 1). Binding of each of the binding partners results in a detectable signal (adapter bound to recognition portion is detected by the particle (i.e., nanoparticle, beads, vesicles) attached to the adapter molecule; target bound to target portion is detected by the

cell attached to the target, or via a further measurable attribute of the target (i.e., biosensor, screen etc., *see* Backer, Figure 1A).

In contrast, embodiments of the present invention provide a two-part presentation system (target moiety and scaffold) where **only** the **target moiety** has a detectable binding partner. **There is no detectable binding partner for the scaffold part of the presentation system** as recited in claim 57. This particular distinction between these two technologies is shown in the illustrations presented below. A side-by-side comparison is also attached herewith.

Backer



Targets:
Receptor
Antigens

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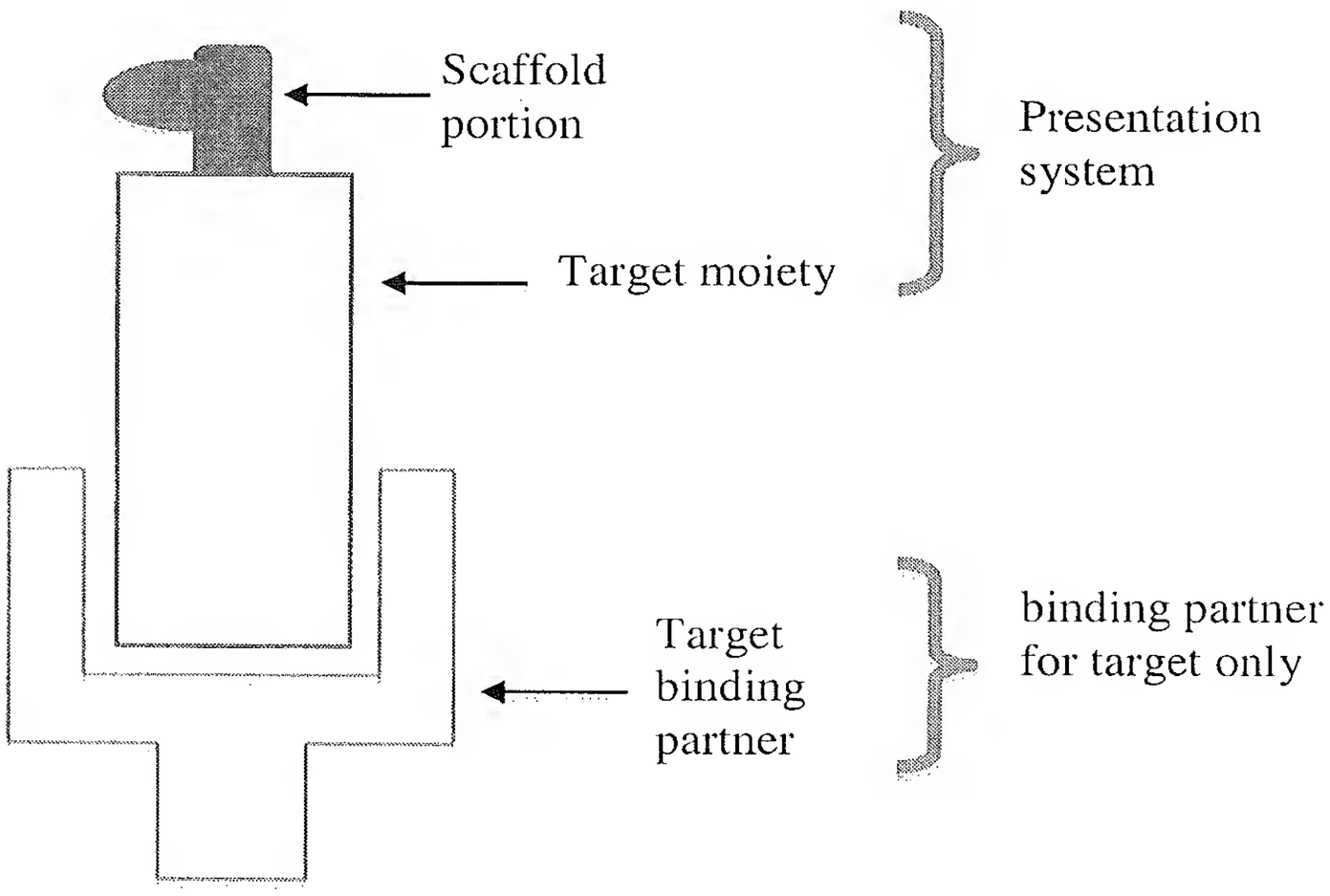

As shown in the illustration, embodiments of the present invention **do not** have a binding partner for the scaffold portion in contrast to the "corresponding" portion of Backer that is active and requires a binding partner.

Prestigiacomo

The Office Action states, "Prestigiacomo et al. teach convalently binding target moiety molecule PSA to ACT. It is noted that the domain of ACT for calibration purpose and would not interact with the binding partner of target molecule. Moreover, the molecular weight of ACT is a controllable property for separation." Office Action, page 3 (citations omitted).

Applicant respectfully submits that Prestigiacomo describes a universal calibration standard for prostate specific antigen (PSA) that is used in the diagnosis of prostate cancer. The calibration standard is a complex between the protein PSA and a partner protein ACT (α_1-antichymotrypsin).

Prestigiacomo differs from embodiments of the present invention in at least that the two components of the Prestigiacomo reference (PSA and ACT) are **natural** proteins that form a **non-covalent complex** (Stenman et al. (1991) A complex between prostate-specific

antigen [PSA] and alpha1-antichymotrypsin [ACT] is the major form of prostate-specific antigen in serum of patients with prostate cancer: assay of the complex improves clinical sensitivity for cancer. Cancer Research 51, 222-226). In contrast, embodiments of the present invention include a two-component presentation system where the two components are **unnatural** and are **covalently** linked. PSA is analogous to a target moiety of embodiments of the present invention, and ACT is analogous to a scaffold material of embodiments of the present invention and do not represent recitations of claim 57.

Accordingly, neither Backer nor Prestigiacomo teach the recitations of claim 57 directed to a **non-natural presentation system**, comprising at least one copy of a target moiety or part thereof that is recognizable by a binding partner and at least one domain of a scaffold material **covalently linked** to said target moiety wherein the scaffold material has a controllable property selected from the group consisting of: (i) molecular weight; (ii) isoelectric point; (iii) number of chemically reactive cysteine amino acid residues; and (iv) number of chemically reactive lysine amino acid residues, wherein the at least one domain of the scaffold is **non-reactive to any detectable binding partner** of the presentation system.

Therefore, Applicant respectfully submits that claim 57 is not anticipated under 35 U.S.C. § 102(b) by Backer or Prestigiacomo, and Applicant respectfully requests that this rejection be withdrawn.

Additionally, not only do the cited references fail to teach the recitations of claim 57, Backer and/or Prestigiacomo fail to suggest the recitations of claim 57. More specifically, one of ordinary skill in the art would recognize that the linkage of PSA to ACT would not form the covalently linked presentation system described by the present application. Instead, a complex mix of products that are **incompatible** with the industrial application and **inconsistent** with the embodiments of the present invention would result– Consequences that the present technology was designed to address.

The amino acid sequence of human PSA and human ACT are shown below, with the chemically reactive residues lysine (K) and cysteine (C) highlighted in green and blue, respectively.

Prostate Specific Antibody (PSA)

Sequence from UniProtKB
P07288

MWVPVVFLTL SVTWIGAAPL ILSRIVGGWE CEKHSQPWQV LVASRGRAVC
GGVLVHPQWV LTAAHCIRNK SVILLGRHSL FHPEDTGQVF QVSHSFPHPL
YDMSLLKNRF LRPGDDSSHD LMLLRLSEPA ELTDAVKVMD LPTQEPALGT
TCYASGWGSI EPEEFLTPKK LQCVDLHVIS NDVCAQVHPQ KVTKFMLCAG
RWTGGKSTCS GDSGGPLVCN GVLQGITSWG SEPCALPERP SLYTKVVHYR
KWIKDTIVAN P

Alpha-1 Antichymotrypsin (ACT)

Sequence from UniProtKB
P01011

MERMLPLLAL GLLAAGFCPA VLCHPNSPLD EENLTQENQD RGTHVDLGLA
SANVDFAFSL YKQLVLKAPD KNVIFSPLSI STALAFLSLG AHNTTLTEIL
KGLKFNLTET SEAEIHQSFQ HLLRTLNQSS DELQLSMGNA MFVKEQLSLL
DRFTEDAKRL YGSEAFATDF QDSAAAKKLI NDYVKNGTRG KITDLIKDLD
SQTMMVLVNY IFFKAKWEMP FDPQDTHQSR FYLSKKKWVM VPMMSLHHLT
IPYFRDEELS CTVVELKYTG NASALFILPD QDKMEEVEAM LLPETLKRWR
DSLEFREIGE LYLPKFSISR DYNLNDILLQ LGIEEAFTSK ADLSGITGAR
NLAVSQVVHK AVLDVFEEGT EASAATAVKI TLLSALVETR TIVRFNRPFL
MIIVPTDTQN IFFMSKVTNP KQA

PSA contains 12 lysine residues and 10 cysteine residues. ACT contains 26 lysine residues and 3 cysteine residues. Attempts to chemically cross-link these two proteins using a strategy employing lysine and/or cysteine residues generally known in the art (e.g. lysine-lysine linkage, or cysteine-cysteine linkage or lysine-cysteine linkage) would be expected to create a huge range of different products. As recognized by one of ordinary skill in the art, such an approach would provide no ability to control the chemical characteristics of the product – which, in contrast, is an aspect of the present technology. As understood by the ordinarily skilled artisan, the cross-linkages would be intramolecular, intermolecular, and/or both. The reaction would result in the polymerization of proteins (PSA-ACT-ACT-PSA-PSA-....., where "–" denotes a covalent bond between components) to create a range of products with hugely different molecular weights, degrees of cross-linkage and other properties. It may even obscure the epitope feature in a proportion of PSA molecules invalidating its use as a calibration standard.

As such, the **non-covalent** PSA-ACT cannot be readily converted to the **covalent** calibration product provided in embodiments of the present invention in a manner that supports a *prima facie* case of obviousness under 35 U.S.C. § 103.

II. Claim Rejection Under 35 U.S.C. §103

Claim 30 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Backer or Prestigiacomo in view of U.S. Patent No. 4,208,479 to Zuk et al. (hereinafter, "Zuk et al."). *See* Office Action, page 4.

For at least the reasons presented above, Backer and Prestigiacomo fail to teach the recitations of claim 57 directed to the non-natural presentation system. The Examiner acknowledges that these references do not explicitly teach a kit comprising the recitations of claim 57. Zuk is cited for the teaching of a kit. However, Applicant respectfully submits that Zuk does not cure the deficiencies of Backer and/or Prestigiacomo regarding the non-natural presentation system. Accordingly, the combination of Backer or Prestigiacomo in view of Zuk fails to teach or suggest the recitations of claim 30.

Therefore, Applicant respectfully submits that claim 30 is not obvious under 35 U.S.C. § 103 in view of Backer or Prestigiacomo in view of Zuk, and Applicant respectfully requests that this rejection be withdrawn.

III. Rejoinder

Applicant respectfully submits that claims 30 and 57 are patentable, and Applicant respectfully requests that some or all of withdrawn claims 31-52 and 54 depending therefrom be rejoined and allowed.

CONCLUSION

Applicant respectfully submits that the present application is in condition for allowance and the same is earnestly solicited. The Examiner is encouraged to telephone the undersigned at 919-854-1400 for resolution of any outstanding issues.

Respectfully submitted,

Shawna Cannon Lemon
Registration No. 53,888

Attachment

USPTO Customer No. 20792
Myers Bigel Sibley & Sajovec, P.A.
P. O. Box 37428
Raleigh, North Carolina 27627
Telephone: (919) 854-1400
Facsimile: (919) 854-1401

CERTIFICATION OF TRANSMISSION

I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on August 11, 2010.

Betty-Lou Medlin